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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/711,476	11/13/2000	C. Thomas Caskey	2875.1001-007	8353

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HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT PAPER NUMBER

1634

DATE MAILED: 06/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/711,476	CASKEY ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 53 is/are allowed.
- 6) ☒ Claim(s) 22-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>04/02/01</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Double Patenting

1. The double patenting rejection is withdrawn in view of the terminal disclaimer filed over claims 1-22 of U.S. Patent No. 6,153,379.

Claim Rejections - 35 USC § 102

2. The rejection of claims 42-50 under 35 U.S.C. 102(e) as being anticipated by Goelet are withdrawn in view of the amendment.
3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 42-51 are rejected under 35 U.S.C. 102(b) and (e) as being anticipated by Soderlund (U.S. Patent 6,013,431) and Soderlund (WO 91/13075).

For ease of reference, the U.S. patent will be referred to for the rejection, but the Soderlund WO is identical in disclosure. This new rejection was necessitated by Applicant's amendment.

Soderlund teaches a method of determining nucleotide identity of at least one nucleotide position of a polynucleotide of interest (see abstract and preamble of claim 1, column 18) comprising the steps of:

a) contacting said polynucleotide of interest with a population of single stranded primers wherein said single stranded primers comprise an array of a set of primers wherein the oligonucleotides are substantially homologous but differ by at least one base at the 3' end (see figures 3, where primers 2 and 3 are identical except for the 3' terminal position and) and where each primer has a known sequence (see figure 3 and columns 9-11, example 1) such that at least one oligonucleotide hybridizes to the polynucleotide of interest immediately adjacent to each nucleotide position of interest (see figure 3 and column 7, lines 29-31) generating single stranded primer complexes (see figure 3 and column 7, lines 49-50) ,

b) subjecting the primer complexes to a single base extension reaction using a polymerase to extend the annealed primers by the addition of a terminating nucleotide, generating an extended primer (see figure 3, where the terminator is ddY1, for example as well as column 8, lines 31-39 and columns 9-11),

c) identifying each terminating nucleotide that has been added to each extended primer, thereby determining the identity of at least one nucleotide position of a polynucleotide of interest (see figure 3 and example 1, columns 9-11).

Soderlund teaches the use of a polymerase and nucleotides corresponding to the four different bases (see column 8, lines 52-58) as well as using multiple differentially labeled nucleotides (see column 8, lines 58-60 and column 19, claim 17). Soderlund teaches the use of fluorescent labels (see column 18, claim 8). Soderlund teaches the use of ddNTPs (see column 18, claim 6). Soderlund teaches primers between 14 and 40 bases (see column 6, lines 42-45) and exemplifies 20 mers (see column 9, line 66,

primer D1, which is 20 nucleotides in length). Soderlund teaches primers of different lengths (see figure 3, primer 1 and primers 2 and 3 are of different lengths).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 22-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goelet et al (U.S. Patent 6,004,744) in view of Rust et al (U.S. Patent 5,605,794).

Goelet teaches a method of analyzing the sequence of a polynucleotide (abstract) comprising the steps: a) contacting a polynucleotide of interest with a population of single stranded primers wherein said population of single stranded primers comprises at least two different oligonucleotides wherein said oligonucleotides have known sequences, such that at least two oligonucleotides hybridize to the

polynucleotide of interest immediately adjacent to one or more nucleotides to be identified to generate template single stranded primer complexes (column 20, example 4 and columns 9-11) , b) subjecting the primer complexes to a single base extension reaction using a polymerase and four nucleotides corresponding to the four bases to extend the annealed primers by the addition of a terminating nucleotide, generating an extended primer (column 20, example 4 and columns 9-11), c) separating said extended primers from each other using gel electrophoresis (column 21, example 4 and columns 9-11), d) identifying each terminating nucleotide that has been added to each extended primer (column 21, example 4, see figure 4, also columns 9-11). Goelet teaches the use of four dideoxynucleotide bases which are differently labeled with different fluorescent labels (column 24, lines 52-67). Goelet teaches detection using both strands, the sense and antisense, to analyze the complimentary polynucleotide of interest (column 23, lines 52-64). Goelet teaches the use of primers which are 21 nucleotides (such as SEQ ID Nos: 13-16). Goelet teaches the use of spectrophotometric detection (column 25, lines 10-14) which includes devices that use CCD or PMT detection processes well known in the art at the time of invention.

While Goelet uses a variety of oligonucleotides of different lengths, Goelet does not expressly teach the use of primers of different lengths.

Rust teaches that for specific detection of nucleotide extension products, "by making use of the fact that the oligonucleotides are discriminated by one more feature. Such a distinction could be, for example, the varying lengths of oligonucleotides of one

set. The extension of different oligonucleotides then produced products of different length (column 11, lines 6-11)".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Goelet with the use of primers of different lengths as taught by Rust, since Rust expressly motivates the use of different length primers in order to achieve specific detection of extension products (column 11, lines 4-11).

Allowable Subject Matter

8. The following is a statement of reasons for the indication of allowable subject matter: Claim 53 is free of the prior art. The claim is drawn to an embodiment in which the oligonucleotide array is regenerated by digestion of the newly added nucleotide after completion of the assay. The cited prior art of Goelet, Rust, or Cantor in the IDS, do not teach regeneration of the array by cleavage mechanisms.

Response to Arguments

9. Applicant's arguments filed May 10, 2002 have been fully considered but they are not persuasive.

Applicant argues that Goelet teaches away from primers of different lengths because Goelet teaches away from the use of gel electrophoresis. This argument is not found persuasive for several reasons. First, as MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 169 USPQ 423 (CCPA 1971)." MPEP 2123 also states "A reference may be relied upon for all that it would have

reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989).” It is clear that simply because Goelet discusses affinity separation as a preferred embodiment, this embodiment does not prevent the use of alternative embodiments or constitute a teaching away from such embodiments such as the gel electrophoresis expressly used by Goelet. It simply teaches Goelet’s preference and does not teach away from other embodiments.

Second, and more importantly, Goelet clearly teaches the use of gel electrophoresis for the separation, showing the express use of gel electrophoresis for the separation at column 21, lines 5-20. This express use of the gel electrophoretic method rebuts the teaching away argument since Goelet demonstrates by example that gel electrophoresis is a desired and useful method in the single nucleotide extension analysis.

Applicant then argues that the teaching of length is somehow “extracted” from the Rust reference. Rust expressly teaches that different lengths are a desirable way to distinguish different primers. This concept was extremely well known in the prior art at the time the invention was made, since the entire basis and point of gel electrophoresis, as opposed to dot blotting, for example, was that gel electrophoresis functions to separate molecules by size. It is hard to overstate how well known it was to the ordinary practitioner in 1992 to select molecules of different size for size based separations in gel electrophoresis. Rust simply evidences that well known fact and provides express motivation to select primers of different sizes.

It is precisely in the context of separation that Rust is used. Rust is addressing the problem of how are different primers able to be distinguished. Goelet uses size separation expressly to distinguish different molecules (see figures 1 and 3, for example). Therefore, when using the size separation of Goulet as in figure 3, the ordinary practitioner would be motivated to ensure the ability to differentially detect the different molecules by using different size primers, as expressly taught and suggested by Rust.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

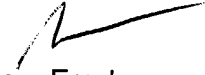
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634

June 4, 2003